



Indium Lung Disease

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e-Appendix 1.

Case H

In 1993, a 37-year old man with a 10 pack-year smoking history established a small ITO production operation. His tasks included mixing indium oxide and tin oxide powders with other chemical compounds, casting the liquid mixture into molds, and firing the castings in a furnace to produce ITO tiles. He primarily handled indium oxide, tin oxide, and ITO, but sometimes worked with other materials, including zinc, aluminum, and antimony. He reported that he did not use respiratory protection in his workplace. Air sampling for indium was not conducted.

After four years as an ITO tile maker, he was told that his chest radiograph was abnormal. After five years as an ITO tile maker, he had the gradual onset of cough without a work-related pattern. A CT scan of the chest demonstrated ground-glass opacities (e-Figure 1A). The etiology of his lung disorder was not determined and his cough persisted.

In 2003, at the age of 47 and after 10 years as an ITO tile maker, the patient was referred to a pulmonologist specializing in occupational lung disease (Dr. Takeuchi). Physical examination revealed normal chest sounds and no clubbing. Laboratory studies were remarkable for elevations in serum concentrations of lactate dehydrogenase (LDH) at 462 IU/L and indium at 92 µg/L (normal <2.0 µg/L). Serum Kerbs von Lungren (KL)-6 was elevated at

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6395 IU/L (normal <500 IU/L). Serum aspartate aminotransferase (AST) was slightly elevated at 42 IU/L. White blood cell count, serum concentrations of C-reactive protein (CRP) and angiotensin converting enzyme (ACE), and titer of antinuclear antibodies (ANA) were not elevated. Pulmonary function tests showed forced vital capacity (FVC) of 89% predicted and a ratio of forced expiratory volume in 1 second (FEV₁) to FVC of 82%.

Chest CT scan in 2003 demonstrated severe fibrosis and some emphysema, with the upper lobes most affected (e-Figures 1B-C). Analysis of bronchoalveolar lavage (BAL) fluid showed an increase in the proportion of lymphocytes at 44%. Surgical lung biopsy revealed interstitial fibrosis and the presence in the alveolar spaces of numerous cholesterol clefts, associated multinucleated giant cells, and in some areas, a proteinaceous exudate (Figure 1D, e-Figures 2A-B). Energy dispersive X-ray analysis of particles noted in the interstitium and alveolar spaces showed indium to be the predominant component. Against medical advice, the patient continued to work as an ITO tile maker. A trial of steroids (prednisolone 30 mg daily) had no therapeutic effect and was discontinued after one month. Chest CT scan in 2009, at the age of 53 and after 16 years as an ITO production worker, was remarkable for worsening of the fibrosis and emphysema (e-Figure 1D). The patient continued to complain of cough.



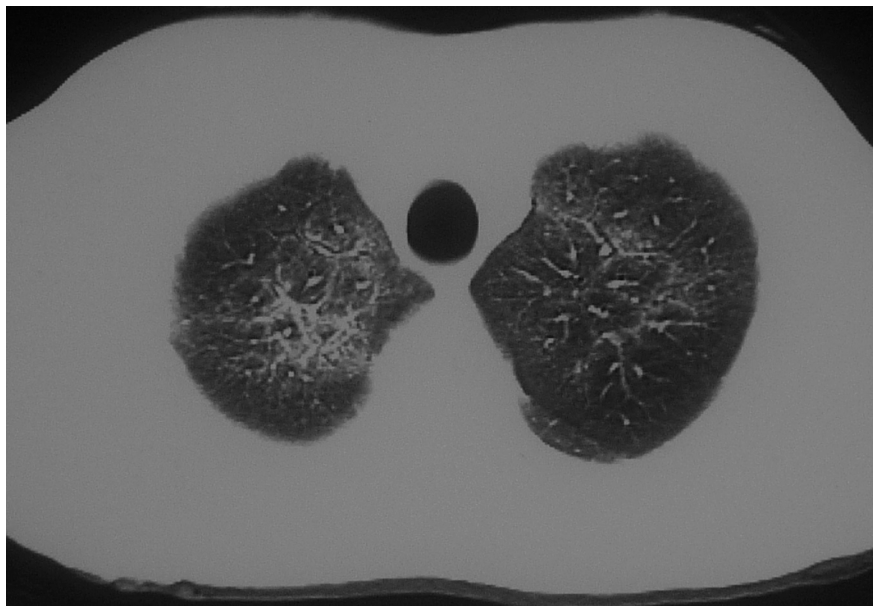
e-FIGURE LEGENDS

e-Figure 1. Case H: Computed tomography scans of the chest showing progression of disease over 11 years. **A.** In 1998 at age 42 years, after 5 years as an indium-tin oxide (ITO) tile maker. Ground-glass opacities are prominent. **B.** and **C.** In 2003 at age 47 years, after 10 years as an ITO tile maker. Findings include severe fibrosis and emphysema in the upper lobes (B) and septal thickening and limited emphysema elsewhere (C). **D.** In 2009 at age 53 years, after 16 years as an ITO tile maker. The upper lobes are remarkable for worsening fibrosis and emphysema, with near-obliteration of normal tissue at this level.

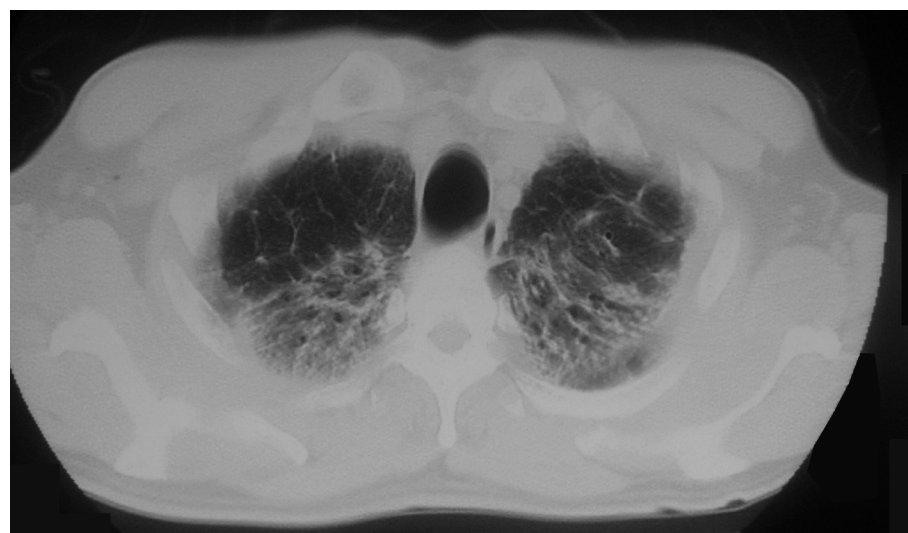
e-Figure 2. Case H: Histopathological sections of lung biopsy. **A.** Low-power overview showing extensive fibrosis and focal honeycombing. **B.** Higher-power magnification showing interstitial fibrosis, acicular cholesterol clefts associated with multinucleated giant cells, and brown particles composed predominantly of indium.



e-Figure 1A.



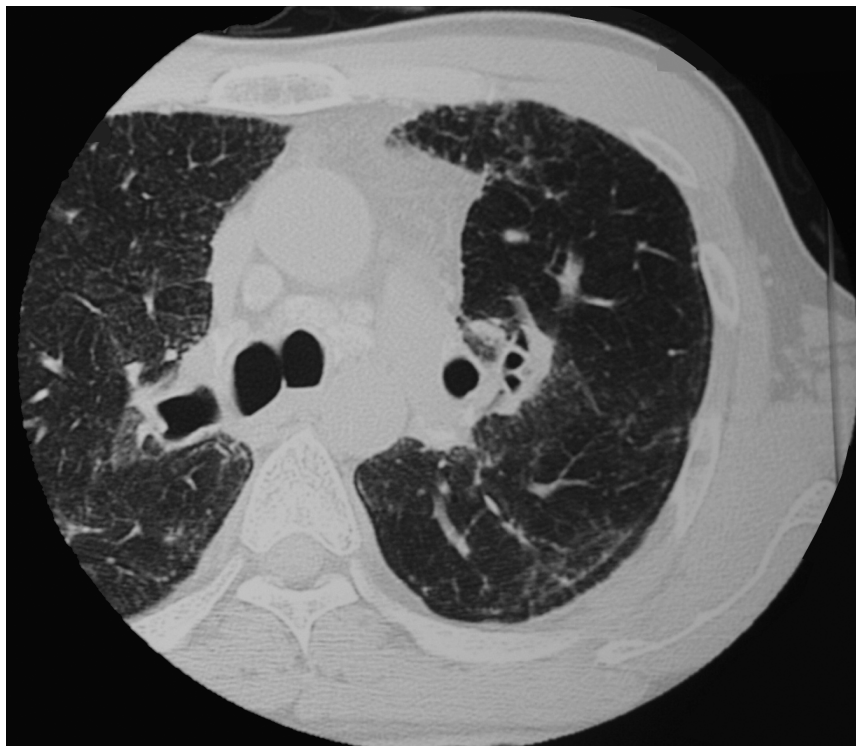
e-Figure 1B.



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e-Figure 1C.



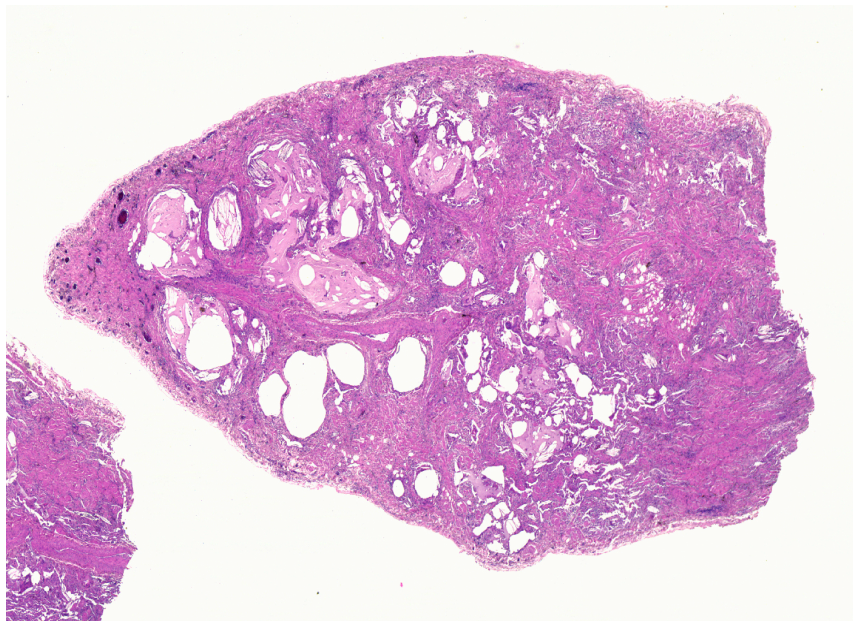
e-Figure 1D.



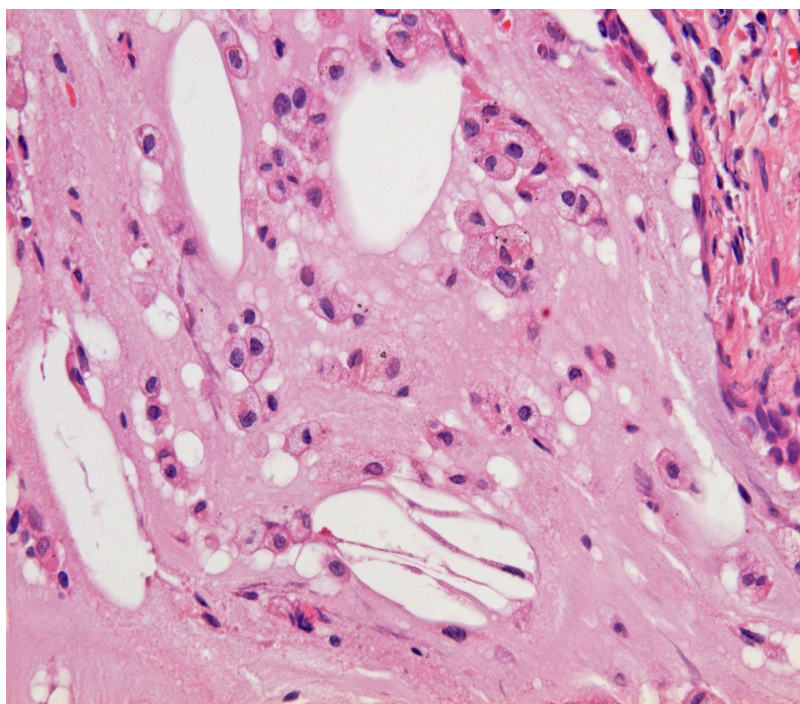
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e-Figure 2A.



e-Figure 2B.



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